III. REMARKS

Claims 1-37 are pending prior to this amendment.

Information Disclosure Statement

Examiner's Comment:

Due to possible errors in the transition from paper files to electronic files, the IDS submitted 17 June 2002 has been only partially considered. No foreign patent documents or non-patent literature has been received. Applicant is kindly requested to re-submit these references for consideration.

Applicant's Response:

In response to the Examiner's request, a supplemental IDS has been filed on December 1, 2004.

Double Patenting

U.S.C. 101.

Examiner's Position:

Claims 19 and 26-36 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 114 and 125-135 of copending Application No. 10/130,559. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Applicant's Response:

Since the conflicting have not yet been patented, this rejection should be held in abeyance.

Rejections

35 USC § 112

Examiner's Position:

Claims 2-4, 6-8, 16, 20, 21, 24-26, and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The wording in claim 2 is allegedly non-sensical and as to what applicant intends. Perhaps the claims should read "the method of claim 1, wherein processing body fluid or tissue samples comprises", if that is what applicant intends to describe.

The method of claims 3 and 4 requires "receiving a body fluid or tissue sample" or "receiving a color image". It is unclear as to where the image is received.

The method of claims 3, 20, 21, and 34 requires "measuring a biologically significant signal level". It is unclear to the Examiner as to the metes and bounds of "biologically significant". The Examiner asks whether there is a certain threshold that defines 'biologically significant'.

Claim 6 recites "whose value of the one coordinate signal lies within a predetermined range". Firstly, the Examiner states it is unclear as to which coordinate the claim refers. The coordinate that represents the Red, Green, Blue (RGB) intensity or a coordinate of the Hue, Luminance, and Saturation (IILS) coordinate recited in claim 5. Secondly, it is unclear as to the parameters of a "predetermined range". The Examiner's question of what range applies also to claims 6,7, 24, and 25.

In regard to the claims 8 and 26 it is unclear to the Examiner as to what is meant by "a

predetermined selection criteria" (Certain color? Size? Shape?).

In regard to claims 16 and 34, the claims recite "processing substantially only rare cell areas". It is unclear to the Examiner, as to the metes and bounds of"substantially". Does this mean that only rare cells are processed? Are other cells processed, as well? Clarification is requested.

Applicant's Response

Claims 1-12, and 19-30 have been canceled without prejudice. Therefore,the rejection of claims 2-4, 6-8, 20, 21, and 24-26 is deemed moot. The rejection of claim 34 has been overcome by replacing the term "biologically significant" with the expression, 'biologically identifying rare cell color image signal'.

35 USC § 102

A. Examiner's Position:

Claims 1-37 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,169,816 B1 (Ravkin).

Specifically, the Examiner alleges that in regard to claims 1, 19, and 37, Ravkin discloses computer implemented imaging a smear of fetal nucleated red blood cells (NRBCs) and other objects, such as red blood cells (RBCs) and white blood cells (WBCs). The objects in the sample are stained selectively for nuclei and fetal hemoglobin in the cytoplasm of fetal NRBCs, such that candidate regions of interest (blobs) are identified for further processing (column 1, lines 65-67 to column 2, lines 1-20). The Examiner further contends that the invention is directed to an evaluation that includes enrichment of fetal NRBCs from maternal blood, positive identification

of fetal NBRCs (signal one), and genetic analysis (signal two) (column 3, lines 3 0-33).

In regard to claims 2, 3, 20, and 21, Ravkin allegedly discloses that a set of features that identify fetal NIRBCs are created to distinguish them from other types of cells, creating contrast in cells containing fetal hemoglobin and another type of contrast in cells having a nucleus. Further analysis of only the region of interest is performed, such that the image falls into a specific class of object (column 7, lines 44-57).

In regard to claims 4-12 and 22-30, the Examiner alleges that the cited reference to Ravkin discloses the image acquisition steps of the instant claims. Thus, separate bright field and fluorescent images are acquired in each field. For the absorption image, the images are balanced so that the background corresponds to mid-gray (column 8, lines 8-30).

In regard to claims 13-16 and 31-34, the Ravkin reference allegedly discloses that upon combining the two images optically, they need to be separated digitally. A background gray level is first determined, the whole field is measured and a histogram of the number of pixels at each possible intensity level is constructed (column 8, lines 31-36), and the histogram is smoothed by adjacent averaging. The intensity corresponding to the top of the highest peak in the histogram is allegedly defined as the background value of light intensity (column 8, lines 36-41). The combined images below-the-background component and above-the background component are compared by the background value to the image on a pixel-by-pixel basis. The Examiner contends that this process is similar to subtraction with saturation producing two separate contrasts dissected from a single image (column 8, lines 42-50).

In regard to claims 17, 18, 35, and 36, the images are allegedly automatically registered, as one image or as separate images (column 9, lines 4-12).

Applicant's Response

Applicant respectfully disagrees. On the contrary, the cited reference to Ravkin neither discloses, claims, nor even suggests the presently claimed invention. Applicant respectfully traverses the Examiner's 35 U.S.C. §102(e) rejections asserting in part that the reference of record does not teach every element of any claim. Applicant respectfully notes that anticipation requires that each and every element of the claimed invention be disclosed in the prior art reference, device, or practice (See, *Akzo N.V. v. U.S. Int'l Trade Comm'n*, 808 F.2d 1471, 1 U.S.P.Q.2d 1241, 1245 (Fed. Cir. 1986).

In the first instance, Applicant has amended the claims herein to streamline prosecution of the claims to embodiments of the invention which are currently believed to be of commercial interest. The cancellation of the claims 1-12, 19-30 and 35, without prejudice, has rendered the rejection under the statute moot.

Applicant fundamentally disagrees with the Examiner's opinion that the reference to Ravkin discloses the computer-controlled method or software product as presently claimed. On the contrary, Applicant respectfully asserts that as each independent claim (and therefore each claim depending from such independent claims) recites the invention, the cited art does not even remotely suggest the computerized analysis of samples of unenriched body fluids as claimed in the independent base claims 38 or 39, as presently presented, let alone through a plurality of computer-aligned microscope objectives to derive digitized large field images. Moreover, Ravkin's dependence on an enrichment step for the preparation of the sample teaches away from the intent and purpose of the instant automatic methodology or program for an "as is" analysis of rare cells in body fluids. It is the unexpected advantage of the presently claimed method or product to to find and characterize the rare cell target at unenriched or original concentrations of as low as 0.000001%. Contrary to the Examiner's construct, the claimed method is distinct and different from the cited reference. In contrast to Ravkin, the automatic computer-controlled microscopic scan of the large field sample to detect the rare cell presence at low magnification

with the aid of a fluorophore illumination and subsequent specific biological identification of the rare cell presence.

Therefore, Applicant respectfully requests that such 35 U.S.C. §102(e) rejections be withdrawn, and the presently pending claims 13-18,31-34, and 36-43 be found allowable.

35 USC 102 (e)

B. Examiner's Position:

In regard to claims 1-4, 19-22, and 37, the Examiner alleges that Tsipouras et al. teach a computerized method of:

(i) receiving a digitized color image of a sample, which has been subjected to fluorescence *in situ* hybridization under conditions to specifically hybridize a fluorophor-labeled probe to a target nucleic acid; (ii) processing the image to separate objects of interest; (iii) measuring parameters in the object of interest to enumerate objects having specific characteristics; and (iv) analyzing the enumeration of objects with respect to a statistically expected enumeration to determine the genetic abnormality (column 3, lines 3 8-48). Fetal cells are analyzed from maternal blood in one embodiment, as described at column 6, lines 1-5. It is further described that RGB color values are used to distinguish different targets, some of which may be labeled by more than one fluorophor (column 12, lines 52-59).

Claims 1-4, 19-22, and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,136,540 (Tsipouras et al.).

According to the Examiner's suggestion, this rejection under 35 U.S.C. 102(e) might be

overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the cited reference was derived from the inventor of this application and thus is not the invention "by another."

Applicant's Response:

The attached Declaration executed by the named inventors, Petros Tsipouras and Trintafyllos P. Tafas, under 37 CFR 1.132, is believed to render this rejection moot since the inventive entity is identical in the cited reference and the instant application.

C. Examiner's Position:

Claims 1-4, 19-22, and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,221,607 B1 (Tsipouras et al.). According to the Examiner's opinion, the applied reference has common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e).

Applicant's Response:

The attached Declaration by the named inventors, Petros Tsipouras and Trintafyllos P. Tafas under 37 CFR 1.132, is believed to render this rejection moot since the inventive entity is the same in the cited reference and the instant application.

In sum, in view of the aforegoing amendment and remarks directed thereto as well as the appropriate Rule 132 affidavits of the inventors, Applicant respectfully assert that the presently entered claims are patentable.

CONCLUSIONS

A good faith effort has been made to place this application in condition for allowance. An early notice of allowance in the next Office action is earnestly requested.

Respectfully submitted,

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